

Case Report

Unusual Case of Coloboma of the Iris with Dextrocardia and Criss Cross Heart Presented Later with Left Sided Diaphragmatic Hernia: First Case Report

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To cite this article:

Sam Hassan, Sameer Sajwani, Pramond Warhekar, Ghassan Nakib, Syed Rizvi. Unusual Case of Coloboma of the Iris with Dextrocardia and Criss Cross Heart Presented Later with Left Sided Diaphragmatic Hernia: First Case Report. *American Journal of Pediatrics*. Vol. 4, No. 4, 2018, pp. 100-103. doi: 10.11648/j.ajp.20180404.15

Received: October 24, 2018; **Accepted:** November 7, 2018; **Published:** December 3, 2018

Abstract: Coloboma of the iris (CI) is an embryonic condition resulted from an incomplete formation of the iris which either presented unilateral or bilateral and as a single eye defect or in association of other eye anomalies. It happens either as an isolated condition or as part of syndromic features or other associations that are well reported in literatures. Coloboma of the iris has been reported in association with diaphragmatic hernia and in some syndromes with dextrocardia. It can happen in families with genetic presentation looks like autosomal dominant pattern, however other genetic pattern were also reported. The combination of CI, dextrocardia, Criss Cross Heart (CCH) which is a rare condition by itself and the congenital diaphragmatic hernia (CDH) has not been reported before. This report is about an unusual case of a boy presented after birth with left sided CI associated with dextrocardia and CCH, who presented later at the age of 16 months with left sided congenital diaphragmatic hernia that was not been diagnosed early. As far as this search for the English literatures concerned, this is the first report of this exclusive association. It is therefore, highly recommended to investigate cases of CI for an associated CDH especially if it is associated with congenital heart defects such as dextrocardia and CCH.

Keywords: Iris Coloboma, Dextrocardia, Diaphragmatic Hernia, Criss Cross Heart

1. Introduction

The typical Coloboma of the iris (CI) results from failure of the embryonic fissure to close in the fifth week of gestation resulting in a "keyhole-shaped" pupil. It may be associated with coloboma of choroid, ciliary body, retina and optic nerve. It can be bilateral or unilateral and will not affect the vision if only involving the iris hence it may remain underdiagnosed. CI may be associated with microphthalmia, cataract, glaucoma, visual acuity problems, nystagmus and retinal detachment. It affects around 1 in 10,000 people and may be caused by many genes most of them yet to be identified. The risk of the CI may be increased by the exposure to environmental factors such as alcohol during pregnancy. Most

often only one individual affected in the family however the affected individual will have the risk of passing the CI to his or her own children. It may be inherited as autosomal dominant, autosomal recessive, X linked dominant or X linked recessive.

CI may present as an isolated anomaly or in association with other syndromes. One of the best known association is, CI and CHARGE syndrome which is acronym for coloboma, heart defect, atresia choanae, retardation of growth, genital defect, and ear abnormalities. CHARGE syndrome is rare with an incidence of 1 in 10,000 newborn births. It happens due to mutation in CHD7 gene that responsible for chromatin remodeling and follows autosomal dominant pattern. CI may be associated with cranial abnormalities such as facial palsy, hearing loss, swallowing difficulties, and smell problems. Affected individuals may have cleft lip and palate and not an

uncommon to have hypogonadotropic hypogonadism with small penis and undescended testis. Less common abnormalities are renal defects, immune system abnormalities, limbs defects, scoliosis and kyphosis.

There are many syndromes where CI may occur as part of them. One of these syndromes is Cat Eye Syndrome (CES) which also known as (Schmid-Fraccaro syndrome). It is a rare syndrome resulted from chromosome 22, inverted duplication (22pter-22q11) or chromosome 22, partial tetrasomy (22pter-22q11) or chromosome 22, partial trisomy (22pter-22q11). Patients with CES may show other abnormalities such as anal, rectal, ears, heart, renal, skeletal, biliary atresia, Hirschsprung disease, cleft lip, cleft palate, short stature, facial mild dysmorphism, microphthalmia, inguinal hernias, hearing loss and diaphragmatic hernia [1].

Other syndrome where CI been has been as an association are, Treacher Collins syndrome, Tilted disc syndrome, Renal coloboma syndrome and mild Noonan phenotype and Patau syndrome (trisomy 13) [2].

In Patau syndrome dextrocardia in isolation or diaphragmatic hernia has been reported in some cases of but not together or with the CI [3]

Criss cross heart (CCH) is extremely rare condition and even more rare to present with dextrocardia. In CCH is a cardiac malformation where the inflow streams of the two ventricles cross due to twisting of the heart about its major axis. The association defect of CCH may happen alone (simple) or in association with corrected transposition of the great arteries and ventricular septal defects. The incidence of CCH is no more than 8 per 1000,000 [4].

In regard to the congenital diaphragmatic hernia (CDH), it is a common congenital defect in newborns that is associated with sever morbidity and mortality. The cause of the CDH is unclear and its pathogenesis is controversial. Recent studies reported genetic pathways which may play role in the development of CDH [5] Around 60% of CDH associated with chromosomal and syndromic anomalies. Chromosomal anomalies are identified in 10 to 20% of prenatally identified cases; the most common diagnoses include trisomies 18, 13, and 21. Other karyotype abnormalities, such as monosomy X, tetrasomy 12 p (isochromosome 12p), partial trisomy 5, partial trisomy 20, and polyploidies, have also been reported [6]. Reported associated anomalies with CDH are many such as Frys syndrome, Fetal alcohol syndrome, De Lange syndrome, CHARGE syndrome, Fraser syndrome, Goldenhar syndrome, Smith-Lemli-Opitz syndrome, multiple pterygium syndrome, Noonan syndrome, and spondylocostal dysostosis. Cardiovascular malformations, urogenital system anomalies, musculoskeletal system defects, and central nervous system were the most common other congenital malformations [7]. There is a wide range of antenatal ultrasound detection sensitivity for CDH [8]. The commonest defect is posteriolateral (Bochdalek) and rarely anterior retrosternal (Morgagni) or central. Herniation usually left sided (80%) and rarely right sided or bilateral with a prevalence of 1-4/10,000 live births.

The congenital diaphragmatic hernia has been reported with

22q11.2 deletion syndrome with cardiac anomalies but not with CI [9] Another syndrome where CI and CDH occur together but not dextrocardia or CCH, is Donnai-Barrow syndrome [10]. It is diagnosed by characteristic clinical features and low-molecular weight proteinuria. The presentation of CI, dextrocardia, CCH and the late presentation of left sided CDH in a normal boy is the first report of such an association in this paper. It highlights the importance of looking to this association in cases presented first with CI after birth.

2. Case Report

A male boy, born at term gestation by normal deliver and uneventful prenatal and postnatal history with a birth weight of 3.10 kg. There were no dysmorphic features. The baby was diagnosed after birth with positional right sided plagiocephaly for which was referred to physiotherapy services. On day 17 of age the patient was noted to have unequal pupil size by his parents and was then diagnosed with left coloboma of the iris by ophthalmologist. The echocardiograph confirmed a dextrocardia, situs solitus with CCH. An abdominal ultrasound reported normal. The child remained well with normal growth and development, the weight following the 5th centiles, the height on 50th centile and the head circumference on 10th centiles. In the first year of life he only had the normal childhood cold symptoms and one time was diagnosed as having bronchiolitis which was treated as an outpatient case with normally recorded oxygen saturation and that resolved without complications.

At the age of 18 months the child had cough and respiratory symptoms due to respiratory syncytial virus bronchiolitis. The chest X Ray showed eventration of the left side of diaphragm with loops of bowel, features consistent with left sided diaphragmatic hernia (figure 1). A CT scan confirmed the left sided CDH (figure 2). The CDH was laparoscopically repaired and the post-surgical CXR showed inflated normal lungs (figure 3). The patient had an uneventful recovery and followed up and was achieving normal growth and development. No chromosomal analysis was done in this case while a hearing test was normal.

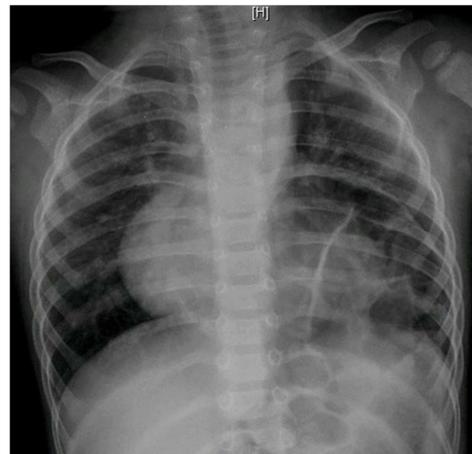


Figure 1. CXR showing left sided eventration with loop of bowels.



Figure 2. CT scan confirmed the L side CDH.

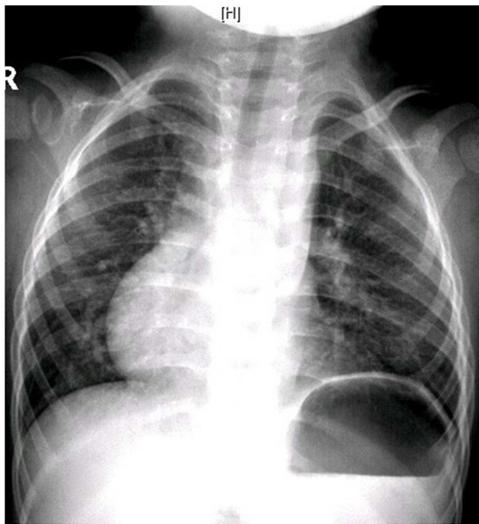


Figure 3. CXR after L CDH repair.

3. Discussion

Coloboma of the iris is a rare congenital abnormality which occur either as an isolated defect inherited usually as autosomal dominant or recessive or may be associated with other anomalies that involve the eyes or the other systems. It is well known association with some syndromes as well as congenital heart defects.

Among the ophthalmic associated abnormalities with CI, microphthalmia, cataract, glaucoma, myopia, nystagmus and retinal detachment are the well-recognized.

A well-known association with CI is CHARGE syndrome which is an autosomal dominant condition, consist of CI, Heart defect, Atresia choanae, Retarded growth and development, Genital hypoplasia, Ear anomalies/deafness, Extremity abnormalities. Gastrointestinal defect associated with CI are, tracheoesophageal fistula, Esophageal atresia, Duodenal atresia, Anal atresia, Anal stenosis, Poor feeding and chewing/swallowing difficulties [11]

Jacobsen syndrome consist of an iris coloboma and other eye defects, annular pancreas and pyloric stenosis but no association with diaphragmatic hernia noted [12]

Meckel gruber syndrome is another syndrome with CI, single umbilical artery, omphalocele, intestinal malrotation and imperforate anus but no CDH [13].

Coloboma of the iris may be part of association with anorectal malformations and gastrointestinal anomalies like malrotations, biliary atresia, duodenal atresia and Hirschsprungs disease but no CDH noted [14]. The other reported association is Renal coloboma syndrome which consist CI with retinal problems, hypoplastic kidneys, cystic kidneys and vesicoureteric reflux [15] but no diaphragmatic hernia noted.

In this case report the CI associated with dextrocardia and CCH. Dextrocardia in general is a rare heart defect. The incidence of dextrocardia associated with situs inversus in the general population is usually 1:10,000, whereas the one associated with situs solitus is 1:30,000 live births and only 1:900,000 in the adult population [16]. It has been described in some anomalies such as Möbius syndrome, Poland anomaly and certain gastrointestinal abnormalities are well recognized with dextrocardia situs inversus but none of them described in literature with dextrocardia solitus and CDH with CI as in this case report [17]. CCH is extremely rare condition and even rarely presented with dextrocardia, this case is the first report of CCH associated with CI, CDH, and dextrocardia.

Congenital Diaphragmatic Hernia (CDH) is caused by a defect in the diaphragm allowing herniation of the abdominal contents such as the intestine, stomach and sometime the liver into the chest. It happen more often in the left side than the right side. The lungs may be hypoplastic and have abnormal vessels that cause respiratory insufficiency and persistent pulmonary hypertension with high mortality. About one third of the cases have cardiovascular malformations and lesser proportions have skeletal, neural, genitourinary, gastrointestinal or other defects. In approximately 60% of cases, CDH is the only birth defect, and these cases are classified as having isolated CDH. Although additional problems commonly coexist with CDH (such as pulmonary hypoplasia, intestinal malrotation, cardiac dextroposition, and left heart hypoplasia. These are usually considered part of a CDH sequence and so their presence does not negate designation of a case as having isolated CDH. The remaining approximately 40% of CDH cases are classified as having CDH + (also referred to as complex, non-isolated, or syndromic CDH) due to the presence of additional major malformations in other organ systems, chromosome abnormalities, or single gene disorders. CDH can be a component of Pallister-Killian, Fryns, Ghersoni-Baruch, WAGR, Denys-Drash, Brachman-De Lange, Donnai-Barrow or Wolf-Hirschhorn syndromes. Some chromosomal anomalies involve CDH as well. The incidence of the CDH is less than 5 in 10,000 live-births [18]. PAGOD syndrome is a severe developmental syndrome characterized by multiple congenital anomalies including cardiovascular defects, pulmonary hypoplasia, diaphragmatic defects and genital anomalies [19]. The PDAC syndrome (pulmonary hypoplasia/agenesis, diaphragmatic hernia/eventration, anophthalmia/microphthalmia, and cardiac defect) and (Spear

syndrome, Matthew-Wood syndrome): report of eight cases including a living child and further evidence for autosomal recessive inheritance [20]. Donnai-Barrow syndrome consist of iris coloboma, diaphragmatic hernia, cardiac abnormalities other than dextrocardia [21]. None of these reports were presented in similar way to this case report.

4. Conclusion

This is a unique case report of a term male presented with CI and dextrocardia with CCH who was presented later at the age of 16 months with CDH that was diagnosed after presentation with respiratory illness. As far as the current English literatures search is concerned no similar report was found. It is therefore assumed that this is the first reported case of such an association. This case report highlights the need for looking of any evidence of diaphragmatic hernia in addition to congenital heart disease when presented with a child with CI after birth. In this case the CDH was overlooked until presented at the age of 16 months with respiratory symptoms.

Acknowledgements

The authors are grateful to the parents of the child who allowed to publish this case and all professionals and departments involved in the management.

Disclosure Policy

All the authors do not have any possible conflicts of interest

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